

1603  
ROPES & GRAY  
ONE INTERNATIONAL PLACE  
BOSTON, MA 02110-2624  
PHONE: (617) 951-7000  
FAX: (617) 951-7050

FAX RECEIVED

DEC 17 2001

GROUP 1600

**FAX TRANSMITTAL LETTER**

OFFICIAL

Total Number of pages including this transmittal letter: **36**

<u>Name</u>	<u>Firm/Company</u>	<u>Fax Number</u>	<u>Phone Number</u>
<b>Examiner Brannock</b>	U.S. Patent & Trademark Office	(703) 308-4242	(703) 306-5876

From: David P. Halstead

**IF YOU DO NOT RECEIVE ALL PAGES, PLEASE CALL IMMEDIATELY AT:****(617) 951-7000****IMPORTANT: PLEASE DELIVER THIS DOCUMENT IMMEDIATELY!**

---

**COMPLETE WHEN SUBMITTING TO FAX DEPARTMENT**

Date: December 14, 2001

Time: 3:48 PM

File Symbol: HMSU-P04-006

Personal ID Number:

Submitted By:

Phone:

---

Comments: **U.S. Application No.: 08/954,771**  
**Filing Date: June 5, 1995**  
**Group Art Unit: 1646**  
**Examiner: M. Brannock**  
**Title: Vertebrate Tissue Pattern Inducing Proteins and Uses Related Thereto**

**THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PERSON TO WHOM IT IS ADDRESSED. IT MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL AND EXEMPT FROM DISCLOSURE UNDER APPLICABLE LAW. If you are not the intended recipient, any dissemination, distribution, copying or use of this document is strictly prohibited. If you have received this communication in error, please notify us by telephone (Collect: ) to arrange for the destruction or return of the original document to us.**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of:  
Ingham et al.

Serial No: 08/954,771

Filed: June 5, 1995

For: Vertebrate Tissue Pattern Inducing  
Proteins and Uses Related Thereto

Attorney Docket No. HMSU-P04-006

Art Unit: 1646

Examiner: M. Brannock

32/4  
B.G.J  
12/17/01

**CERTIFICATE OF FACSIMILE**

I hereby certify that this correspondence is being transmitted by facsimile in the United States Patent and Trademark Office on the date indicated below:

December 14, 2001

Date of Signature  
and of Mail Deposit

  
Karen DiRocco

Assistant Commissioner of Patents  
Washington, D.C. 20231

**REPLY UNDER 37 CFR 1.111**

Sir:

This amendment is being filed in reply to the outstanding Office Action, mailed September 24, 2001, in connection with the above application. Please enter the following amendments:

**In the specification:**

On page 142, please replace the last paragraph with:

I  
Various fragments of the mouse *Shh* gene were cloned into the pET11D vector as fusion proteins with a poly(His) leader sequence to facilitate purification. Briefly, fusion genes encoding the mature M-*Shh* protein (corresponding to Cys-25 through Ser-437 of SEQ ID No. 11) or N-terminal containing fragments, and an N-terminal exogenous leader having the sequence M-G-S-S-H-H-H-H-H-L-V-P-R-G-S-H-M (SEQ ID No. 47) were cloned in pET11D and introduced into *E. coli*. The poly(His)-*Shh* fusion proteins were purified using nickel chelate chromatography according to the vendor's instructions (Qiagen catalog 30210), and the poly(His) leader cleaved from the purified proteins by treatment with thrombin.

12/18/2001 61RAMEL 00000003 181945 08954771  
01 FC:116 400.00 CH